

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re CONTINUATION
PATENT APPLICATION of

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Usha KASID et al.

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Group Art Unit: Unassigned

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Application Serial No.: (Unassigned)

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Examiner: Unassigned

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Filed: August 16, 2001

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Title: **LIPOSOMES CONTAINING OLIGONUCLEOTIDES**

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**PRELIMINARY AMENDMENT AND
RESPONSE TO OFFICE ACTION IN PARENT APPLICATION**

Hon. Commissioner of Patents
Washington, DC 20231

Sir:

In complete response to the final rejection dated September 11, 2000, in parent application no. U.S. Serial No. 09/354,109, Applicants submit herein the following remarks and reminders.

Applicants note at the outset that these amendments, in large part, conform the scope of the claims to that allowed in U.S. Serial No. 09/982,084.

IN THE SPECIFICATION

Page 1, before paragraph 1, insert the following:

--Cross Reference to Related Applications:

This patent document is a continuation of U.S. Patent Application No. 09/354,109 filed July 15, 1999, which is a divisional application of U.S. Patent Application No. 08/957,327 filed October 24, 1997, the content of which is incorporated herein by reference in its entirety.--

IN THE CLAIMS

Kindly cancel all of pending claims 18-20, 23, 25, 27-33 and substitute the following:

--34. An improved method of treating a patient having cancerous tumor tissue comprising the administration of therapeutic radiation wherein the improvement comprises sensitizing said cancerous tumor tissue by the administration of a radiosensitizing composition comprising a cationic liposome, phosphatidylcholine and cholesterol which cationic liposome has encapsulated therein an antisense oligonucleotide of no more than 40 bases that specifically binds to an oncogene nucleic acid sequence expressed by said tumor tissue.

35. The method of Claim 34, wherein the oncogene is selected from the group consisting of ras, raf, cot, mos and myc.

36. The method of Claim 35, wherein the oncogene is raf-1.

37. The method of Claim 34, wherein said tumor tissue is a solid tumor.

38. The method of Claim 34, wherein said tumor is a laryngeal squamous carcinoma.

39. The method of Claim 39, wherein radiation and said cationic liposome are administered together.

40. The method of Claim 39, wherein said radiation and cationic liposome are administered separately.

41. The method of Claim 40, wherein said cationic liposome is administered prior to the radiation.

REMARKS

Based on the following, reconsideration and re-examination of the subject invention, pursuant to and consistent with 37 CFR 1.112, and in light of the remarks which follow, are respectfully requested.

Essentially, Applicants respectfully maintain that sufficient evidence has been submitted which substantiates the novel, non-obvious features of the invention, and also with respect to the efficacy of the claimed method.

As previously argued, the present inventors have surprisingly discovered that particular cationic liposomol formulations containing antisense oligos which are specific to oncogenes expressed by tumor tissue, when administered to patients undergoing radiotherapy, renders tumor cells more susceptible to radiotherapy. While not wanting to be bound by their belief, it is hypothesized that the oligo containing cationic liposomal formulations renders tumor cells more susceptible to apoptosis, perhaps by triggering the expression of "death" genes.

Applicants note that with respect to such discovery, the Examiner has acknowledged the inventiveness of this invention in the context of one antisense oligonucleotide, which is specific to raf-1. The only aspect wherein the subject claims are broader than that allowed in the parent application resides in the fact that the claims generically encompass the use of antisense oligos targeted against an oncogene expressed by a particular tumor.

With respect thereto, as the Examiner can well appreciate, the use of antisense therapy to treat cancerous tumors is hardly novel. As evidence of this fact, Applicants note that a search of the U.S. Patent database revealed that 59 patents have issued from 1996 to the present date containing claims directed to antisense therapy of cancer.

Of these patents, one is believed to be directly on point to the facts at hand. Specifically, U.S. Patent 6,165,440 issued December 26, 2000 is directed toward a method for enhancing the delivery of an anti-cancer drug to a solid tumor by injecting nanoparticles or microparticles into the tumor by IV administration and irradiation, with administration of an anti-cancer drug. Moreover, of the list of suitable anti-cancer drugs in the claims, anti-sense oligos are specifically included.

Presumably there, the Examiner properly concluded that the Patentee therein was entitled broad scope with respect to the anti-cancer drug as this did not constitute the significant novel and non-obvious aspect of the invention. Rather, the generic discovery of their patented invention involved a novel therapeutic combination that potentiated efficacy.

The present specification involves a very similar set of facts. Essentially, the present inventors have discovered that a particular cationic liposomal delivery system potentiates the efficacy of an antisense oligos, particularly by allowing for the specific internalization of

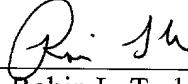
tumor cells that express a gene bound by said oligo. Thereby such cells are rendered more susceptible to radiotherapy.

This enhancement has been demonstrated both in vitro and in vivo, in an accepted tumor model, and in ongoing human clinical studies. In view of this surprising and beneficial discovery, Applicants respectfully submit that it would be unreasonable and unfair to limit the scope of the allowed claims to a particular antisense oligo, especially as numerous patents have issued to date, substantiating the growing acceptance by the Patent Office, and those skilled in the art, that antisense oligo therapy is effective.

Therefore, based on the foregoing, the Examiner is respectfully requested to reconsider the propriety of the rejection, especially since it does not take into sufficient account the full scope of the discovery made by Applicants.

Respectfully submitted,

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